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* * * * * * * * * *   Welcome to STN International   * * * * * * * * * *
* * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * *

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L1      STRUCTURE UPLOADED

=> dis l1
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L1               STR
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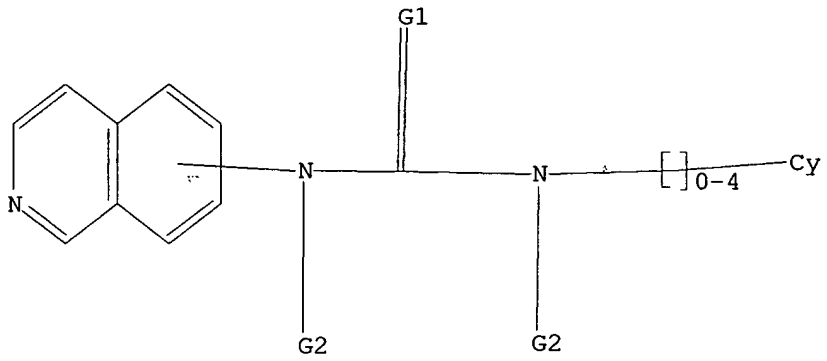


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G1 O,S,N
G2 Ak,H


Structure attributes must be viewed using STN Express query preparation.


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L2            2 SEA SSS SAM L1

=> s l1 full
L3           38 SEA SSS FUL L1

=> file caplus

=> s l3
L4           21 L3

=> dis 1-21 bib abs hitstr

L5   ANSWER 1 OF 21  CAPLUS  COPYRIGHT 2006 ACS on STN
AN   2005:1262710  CAPLUS
DN   144:22817
TI   Preparation of phenyl or pyridinyl ureas as antagonists of P2Y1 receptors
     for the treatment of thromboembolic disorders
IN   Chao, Hannguang J.; Tuerdi, Huji; Herpin, Timothy; Roberge, Jacques Yves;
     Liu, Yalei; Lawrence, R. Michael; Rehfuss, Robert P.; Clark, Charles G.;
     Qiao, Jennifer X.; Gungor, Timur; Lam, Patrick Y. S.; Wang, Tammy C.;
     Ruel, Rejean; L'Heureux, Alexandre L.; Thibeault, Carl; Bouthillier,
     Gilles; Schnur, Dora M.
```

PA Bristol-Myers Squibb Company, USA
SO PCT Int. Appl., 343 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2005113511 | A1 | 20051201 | WO 2005-US16422 | 20050511 |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| | RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | US 2005267119 | A1 | 20051201 | US 2005-126915 | 20050511 |
| PRAI | US 2004-570288P | P | 20040512 | | |
| | US 2005-665735P | P | 20050328 | | |
| | US 2005-665817P | P | 20050328 | | |

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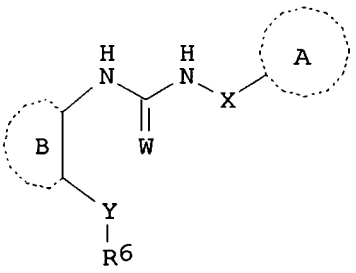
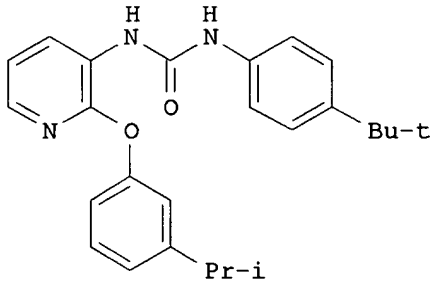



I



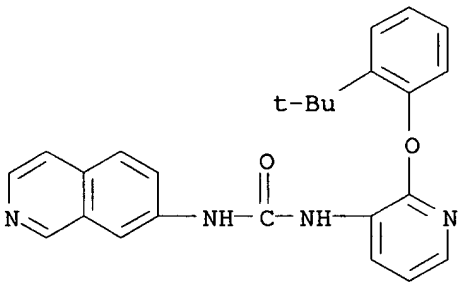

II

AB Title compds. I [wherein ring A = (un)substituted aryl or heterocyclyl; ring B = (un)substituted heteroaryl; W = O or S; X = bond or (un)substituted alkylene; Y = O, S, NH, etc.; R6 = Ph, phenylalkyl, etc., and stereoisomers, pharmaceutically acceptable salts or solvates thereof] were prepared as P2Y1 receptor inhibitors. For instance, etherification of m-isopropylphenol with 2-chloro-3-nitropyridine at 180°C for 700 s in a microwave (87% yield) followed by hydrogenation in the presence of Pd/C (90% yield) gave a pyridinamine, which underwent nucleophilic addition with p-tert-butylphenyl isocyanate to afford urea II (30% yield). Some compds. I have been identified to exhibit Ki's of ≤ 10 mM in the P2Y1 binding assay. I and their pharmaceutical compns. are useful in treating diseases responsive to modulation of P2Y1 receptor activity, such as thromboembolic disorders (no data).

IT **870544-95-9P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU

(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(inhibitor; preparation of Ph or pyridinyl ureas as antagonists of P2Y1 receptors for the treatment of thromboembolic disorders)

RN 870544-95-9 CAPLUS
CN Urea, N-[2-[2-(1,1-dimethylethyl)phenoxy]-3-pyridinyl]-N'-7-isoquinolinyl- (9CI) (CA INDEX NAME)

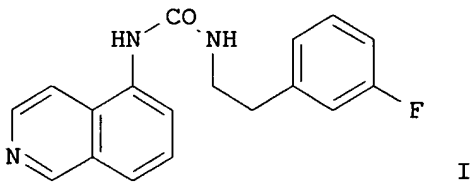



RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:450974 CAPLUS
DN 142:481963
TI Preparation of used azabicyclic compounds that inhibit vanilloid receptor subtype 1 (VR1) receptor
IN Lee, Chih-Hung; Bayburt, Erol K.; DiDomenico, Stanley; Drizin, Irene; Gomtsyan, Arthur R.; Koenig, John R.; Perner, Richard J.; Schmidt, Robert G.; Turner, Sean C.; Jinkerson, Tammie K.; Zheng, Guo Zhu
PA USA
SO U.S. Pat. Appl. Publ., 94 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI US 2005113576 | A1 | 20050526 | US 2004-911019 | 20040804 |
| PRAI US 2003-492528P | P | 20030805 | | |

OS MARPAT 142:481963
GI




I

AB Azabicyclic compds., such as R-X5-C(:Z1)-Z2-L-R9 [R = substituted or unsubstituted azabicyclyl moiety, such as 5-isoquinolinyl, 4-indazolyl, 4-indolyl or 5-cinnolinyl; X5 = -N(R8a)-, -C(R8a)(R8b)-; Z1 = O, NH, S; Z2

= bond, -NH-, -O-; L = alkylene, alkenylene, alkynylene, cycloalkylene; R8a = H, alkyl; R8b = H, OH, halogen, alkyoxy, alkoxycarbonylalkyl, alkylcarbonyloxy, alkylsulfonyloxy; R9 = aryl], were prepared for use in pharmaceutical compns. as VR1 antagonists for treating a disorder wherein the disorder is ameliorated by inhibiting a VR1 receptor, such as pain, inflammatory thermal hyperalgesia, urinary incontinence and bladder overactivity. Thus, N-[2-(3-fluorophenyl)ethyl]-N'-isoquinolin-5-ylurea (I) was prepared starting from 5-isoquinolinamine, Cl3CCOCl and F-3-C6H4(CH2)2NH2 via urea formation in 65% yield refluxing F-3-C6H4(CH2)2NH2 and 2,2,2-trichloro-N-5-isoquinolinylacetamide in MeCN using DBU. The prepared azabicyclic compds. were tested in vivo to determine their antinociceptive effect in male mice.

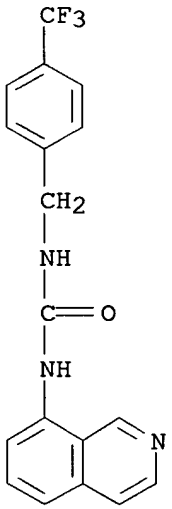
IT **581810-21-1P 581810-22-2P**

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of fused azabicyclic compds. that inhibit vanilloid subtype 1 (VR1) receptor)

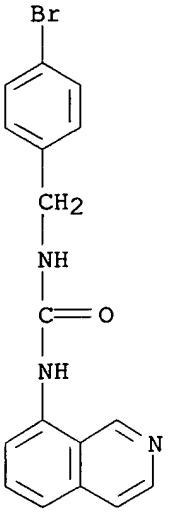
RN 581810-21-1 CAPLUS

CN Urea, N-8-isoquinolinyl-N'-[[4-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)

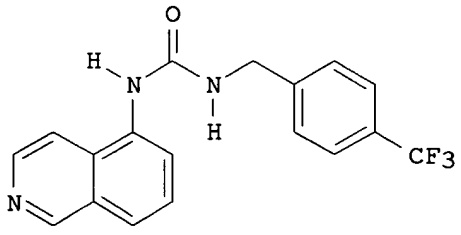


RN 581810-22-2 CAPLUS

CN Urea, N-[(4-bromophenyl)methyl]-N'-8-isoquinolinyl- (9CI) (CA INDEX NAME)



L5 ANSWER 3 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:31491 CAPLUS
DN 142:240400
TI Novel transient receptor potential vanilloid 1 receptor antagonists for the treatment of pain: Structure-activity relationships for ureas with quinoline, isoquinoline, quinazoline, phthalazine, quinoxaline, and cinnoline moieties
AU Gomtsyan, Arthur; Bayburt, Erol K.; Schmidt, Robert G.; Zheng, Guo Zhu; Perner, Richard J.; Didomenico, Stanley; Koenig, John R.; Turner, Sean; Jinkerson, Tammie; Drizin, Irene; Hannick, Steven M.; Macri, Bryan S.; McDonald, Heath A.; Honore, Prisca; Wismer, Carol T.; Marsh, Kennan C.; Wetter, Jill; Stewart, Kent D.; Oie, Tetsuro; Jarvis, Michael F.; Surowy, Carol S.; Faltynek, Connie R.; Lee, Chih-Hung
CS Global Pharmaceutical Research and Development, Abbott Laboratories, Abbott Park, IL, 60064, USA
SO Journal of Medicinal Chemistry (2005), 48(3), 744-752
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
OS CASREACT 142:240400
GI



I

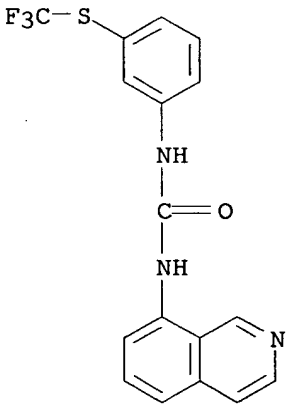
AB Transient receptor potential vanilloid 1 (TRPV1) receptor antagonists with

various bicyclic heteroarom. pharmacophores were synthesized, and their in vitro activity in blocking capsaicin activation of TRPV1 was assessed. On the basis of the contribution of these pharmacophores to the in vitro potency, they were ranked in the order of 5-isoquinoline > 8-quinoline = 8-quinazoline > 8-isoquinoline ≥ cinnoline ≈ phthalazine ≈ quinoxaline ≈ 5-quinoline. The 5-isoquinoline-containing compound I (hTRPV1 IC50 = 4 nM) exhibited 46% oral bioavailability and in vivo activity in animal models of visceral and inflammatory pain. Pharmacokinetic and pharmacol. properties of I were substantial improvements over the profile of the high-throughput screening hit (hTRPV1 IC50 = 22 nM), which was not efficacious in animal pain models and was not orally bioavailable.

IT **845509-36-6P**
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation, transient receptor potential vanilloid 1 receptor affinity, and structure-activity relationship of ureas with quinoline, isoquinoline, quinazoline, phthalazine, quinoxaline, and cinnoline moieties and isoquinolin carbamates)

RN 845509-36-6 CAPLUS

CN Urea, N-8-isoquinolinyl-N'-[3-[(trifluoromethyl)thio]phenyl]- (9CI) (CA INDEX NAME)




RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:1080867 CAPLUS
DN 142:56195
TI Preparation of isoquinolinecarboxamides and their use in mediating hypoxia inducible factor and increasing endogenous erythropoietin
IN Arend, Michael P.; Flippin, Lee A.; Guenzler-Pukall, Volkmar; Ho, Wen-Bin; Turtle, Eric D.; Du, Xiaohui
PA Fibrogen, Inc., USA
SO PCT Int. Appl., 302 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|

PI WO 2004108681 A1 20041216 WO 2004-US17773 20040604
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
US 2004254215 A1 20041216 US 2004-861082 20040604
PRAI US 2003-476420P P 20030606
US 2003-476519P P 20030606
US 2003-476633P P 20030606
US 2003-476811P P 20030606
OS MARPAT 142:56195
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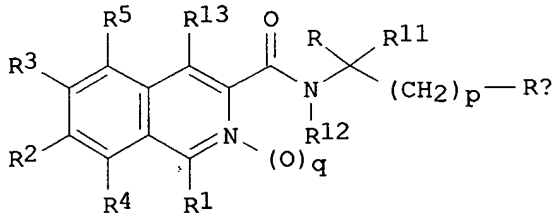


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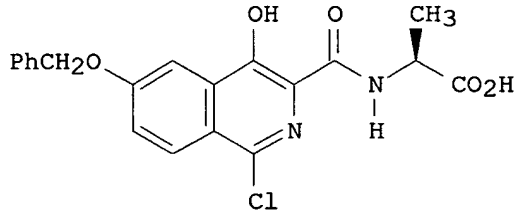



II

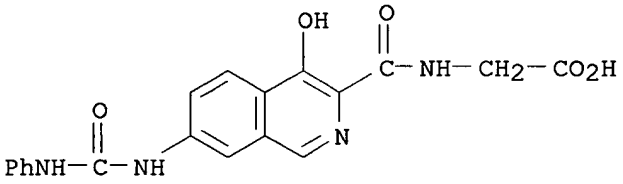
AB Title compds. I [ wherein q = 0 or 1; p = 0 or 1; Ra = COOH or -WR8; W = O, S(O)n or NR9; R8, R9 = H, (un)substituted alkyl or (hetero)aryl; n = 0-2; R1 = H, (un)substituted alk(yl/oxy), amino or sulf(a/i/o)nyl; R2, R3 = H, (un)substituted alk(yl/oxy), (hetero)aryl, aryloxy, sulf(a/i/o)nyl, halo, OH or cyano; R4, R5 = H, halo, (un)substituted alk(yl/oxy) or (hetero)aryl, R = H, D or Me; R11 = H, D or (un)substituted alkyl; R12 = H or alkyl; R13 = H, (un)substituted (cyclo)alkoxy or aryloxy; et al., with some limitations, and pharmaceutically acceptable salts, esters and prodrugs thereof] were prepared For example, 6-benzyloxy-1-chloro-4-hydroxyisoquinoline-3-carboxylic acid underwent HATU-mediated coupling reaction with L-alanine Me ester hydrochloride followed by basic hydrolysis to give compound II. I were reported to be active in several biol. assays (no data). Compds. I and their pharmaceutical compns. are useful in mediating hypoxia inducible factor (HIF) and in treating erythropoietin-associated conditions, such as anemic and neurol. disorders,

by increasing endogenous erythropoietin.

IT **808119-10-0P**, [[[4-Hydroxy-7-(3-phenylureido)isoquinolin-3-yl]carbonyl]amino]acetic acid **808119-13-3P**, [[[4-Hydroxy-6-(3-phenylureido)isoquinolin-3-yl]carbonyl]amino]acetic acid
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of isoquinolinecarboxamides as modulators of hypoxia inducible factor and endogenous erythropoietin)

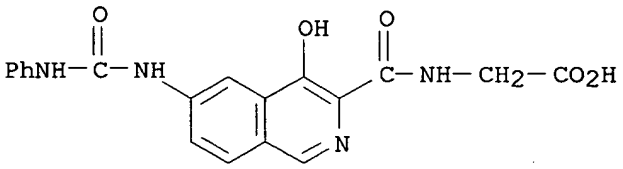
RN 808119-10-0 CAPLUS

CN Glycine, N-[[4-hydroxy-7-[[(phenylamino)carbonyl]amino]-3-isoquinolinyl]carbonyl]- (9CI) (CA INDEX NAME)



RN 808119-13-3 CAPLUS

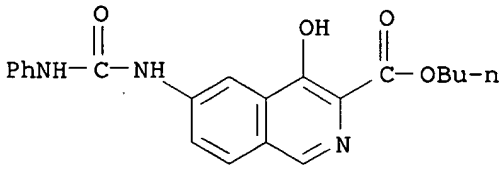
CN Glycine, N-[[4-hydroxy-6-[[(phenylamino)carbonyl]amino]-3-isoquinolinyl]carbonyl]- (9CI) (CA INDEX NAME)



IT **808119-11-1P**, 6-(3-Phenylureido)-4-hydroxyisoquinoline-3-carboxylic acid butyl ester **808119-12-2P**, 7-(3-Phenylureido)-4-hydroxyisoquinoline-3-carboxylic acid butyl ester
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of isoquinolinecarboxamides as modulators of hypoxia inducible factor and endogenous erythropoietin)

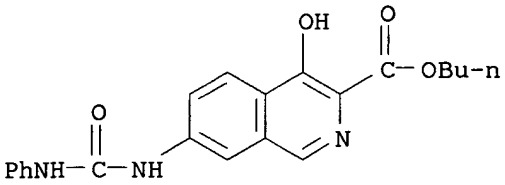
RN 808119-11-1 CAPLUS

CN 3-Isoquinolinecarboxylic acid, 4-hydroxy-6-[[(phenylamino)carbonyl]amino]-, butyl ester (9CI) (CA INDEX NAME)



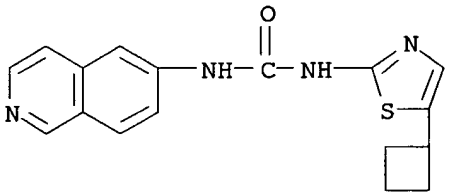
RN 808119-12-2 CAPLUS

CN 3-Isoquinolinecarboxylic acid, 4-hydroxy-7-[[(phenylamino)carbonyl]amino]-, butyl ester (9CI) (CA INDEX NAME)



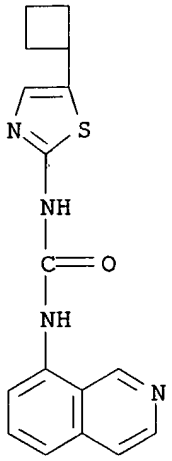
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 5 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:863096 CAPLUS
DN 142:231
TI Discovery and SAR of 2-aminothiazole inhibitors of cyclin-dependent kinase 5/p25 as a potential treatment for Alzheimer's disease
AU Helal, Christopher J.; Sanner, Mark A.; Cooper, Christopher B.; Gant, Thomas; Adam, Mavis; Lucas, John C.; Kang, Zhijun; Kupchinsky, Stanley; Ahlijanian, Michael K.; Tate, Bonnie; Menniti, Frank S.; Kelly, Kristin; Peterson, Marcia
CS Neuroscience Medicinal Chemistry and Pharmacology, Pfizer Global Research and Development, Groton, CT, 06340, USA
SO Bioorganic & Medicinal Chemistry Letters (2004), 14(22), 5521-5525
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier B.V.
DT Journal
LA English
OS CASREACT 142:231
AB High-throughput screening with cyclin-dependent kinase 5 (cdk5)/p25 led to the discovery of N-(5-isopropyl-thiazol-2-yl)isobutyramide. This compound is an equipotent inhibitor of cdk5 and cyclin-dependent kinase 2 (cdk2)/cyclin E (IC50 = ca. 320 nM). Parallel and directed synthesis techniques were utilized to explore the SAR of this series. Up to 60-fold improvements in potency at cdk5 and 12-fold selectivity over cdk2 were achieved.
IT **474460-64-5P 474461-02-4P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(aminothiazole inhibitors of cyclin-dependent kinase)
RN 474460-64-5 CAPLUS
CN Urea, N-(5-cyclobutyl-2-thiazolyl)-N'-6-isoquinolinyl- (9CI) (CA INDEX NAME)



RN 474461-02-4 CAPLUS
CN Urea, N-(5-cyclobutyl-2-thiazolyl)-N'-8-isoquinolinyl- (9CI) (CA INDEX

NAME)

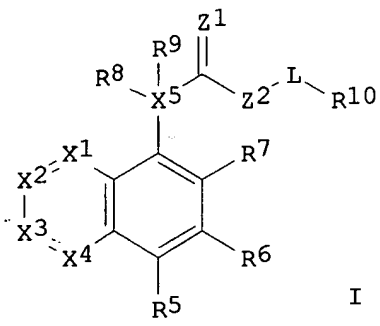


RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 6 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:652634 CAPLUS
DN 141:174087
TI Preparation of fused azabicyclic compounds that inhibit vanilloid receptor subtype 1 (VR1)
IN Lee, Chih-Hung; Bayburt, Erol K.; Didomenico, Stanley; Drizin, Irene; Gomtsyan, Arthur R.; Koenig, John R.; Perner, Richard J.; Schmidt, Robert G.; Turner, Sean C.; White, Tammie K.; Zheng, Guo Zhu
PA Abbott Laboratories, USA
SO U.S. Pat. Appl. Publ., 93 pp., Cont.-in-part of U.S. Ser. No. 364,210.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 3

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | US 2004157849 | A1 | 20040812 | US 2003-634678 | 20030805 |
| | US 6933311 | B2 | 20050823 | | |
| | US 2003158198 | A1 | 20030821 | US 2003-364210 | 20030211 |
| | WO 2005016890 | A1 | 20050224 | WO 2004-US25109 | 20040804 |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| | RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| PRAI | US 2003-364210 | A2 | 20030211 | | |
| | US 2002-358220P | P | 20020220 | | |
| | US 2003-634678 | A | 20030805 | | |

OS MARPAT 141:174087
GI



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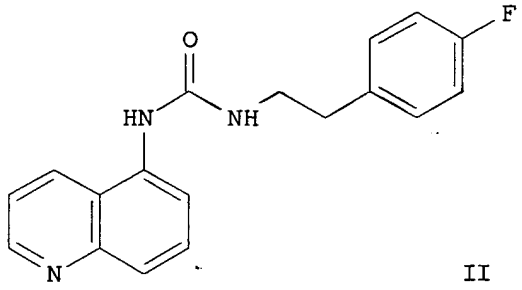


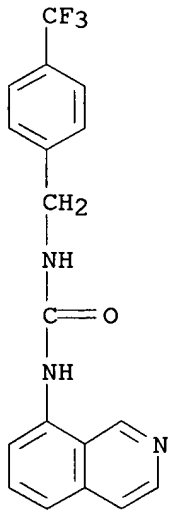
II

AB Compds. of formula I [X1-X5 = (substituted) N, (substituted) CH; Z1 = O, NH, S; Z2 = bond, NH, O; L = alkylene, cycloalkylene, piperazinediyl, etc.; R5-R9 = H, alkyl, alkenyl, alkoxy, carboxy, cycloalkyl, formyl, mercapto, etc.; R10 = H, aryl, cycloalkyl, heterocyclyl] are prepared as vanilloid receptor subtype 1 (VR1) antagonists that are useful in treating pain, inflammatory thermal hyperalgesia, urinary incontinence and bladder overactivity. Thus, II was prepared from 5-aminoisoquinoline and 2-(3-fluorophenyl)ethylamine. The prepared compds. were found to be antagonists of VR1 with IC50 of 0.1 nM to 1000 nM.

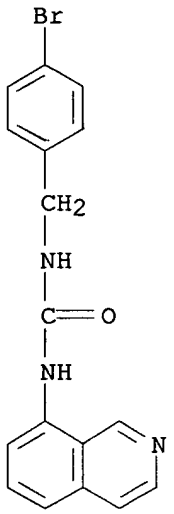
IT **581810-21-1P 581810-22-2P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of fused azabicyclic compds. as vanilloid receptor 1 inhibitors)

RN 581810-21-1 CAPLUS

CN Urea, N-8-isoquinolinyl-N'-[[4-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)



RN 581810-22-2 CAPLUS
CN Urea, N-[(4-bromophenyl)methyl]-N'-8-isoquinolinyl- (9CI) (CA INDEX NAME)



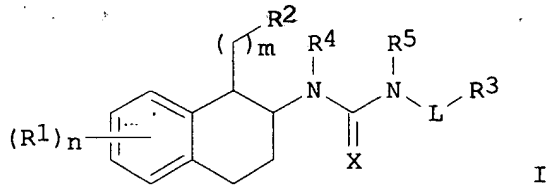

L5 ANSWER 7 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:931319 CAPLUS
DN 140:4865
TI Aminotetralin-derived urea modulators of vanilloid VR1 receptor useful for treatment of pain, inflammation, etc.
IN Codd, Ellen; Dax, Scott L.; Jetter, Michele; Mcdonell, Mark; Mcnally, James J.; Youngman, Mark
PA Janssen Pharmaceutica N.V., Belg.
SO PCT Int. Appl., 206 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2003097586 | A1 | 20031127 | WO 2003-US15254 | 20030515 |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | CA 2486092 | AA | 20031127 | CA 2003-2486092 | 20030515 |
| | US 2003236280 | A1 | 20031225 | US 2003-438477 | 20030515 |
| | US 6984647 | B2 | 20060110 | | |
| | EP 1506166 | A1 | 20050216 | EP 2003-731189 | 20030515 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| | JP 2005526137 | T2 | 20050902 | JP 2004-505319 | 20030515 |

| | | | | | |
|---|---|---|---|---|---|
| | US 2005187291 | A1 | 20050825 | US 2005-45956 | 20050128 |
| PRAI | US 2002-381575P | P | 20020517 | | |
| | US 2003-438477 | A3 | 20030515 | | |
| | WO 2003-US15254 | W | 20030515 | | |

OS MARPAT 140:4865


GI



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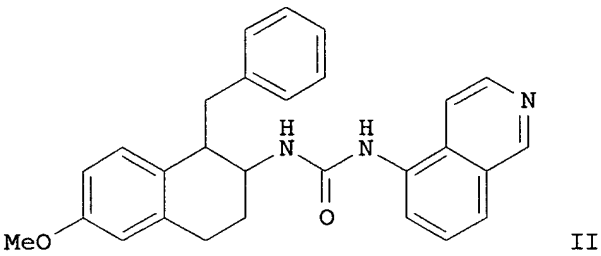
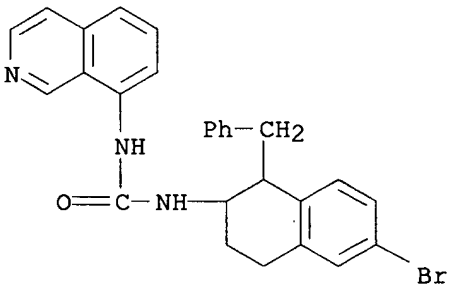


II


AB The invention is directed to vanilloid receptor VR1 ligands I [R1 = H, OH, halo, (un)substituted alkyl, alkoxy, fluoroalkyl, fluoroalkoxy, alkylthio, cycloalkyl, cycloalkoxy, or Ph, NO2, (di)(alkyl)amino, cycloalkylamino, cyano, CO2H, alkoxycarbonyl, aroyl, carbamoyl, amidino, etc.; n = 1-3; m = 0-3; R2 = H, OH, alkyl, alkenyl, alkylidenyl, alkylidynyl, F, Cl, cycloalkyl, (un)substituted Ph, naphthyl, OPh, or heteroaryl; L = bond, alkanediyl, alkenediyl, alkynediyl, cycloalkanediyl; R3 = (un)substituted Ph, naphthyl, or heteroaryl; R4, R5 = H, alkyl; X = O, S; including enantiomers, diastereomers, tautomers, solvates, and/or pharmaceutically acceptable salts]. More particularly, the invention relates to β-aminotetralin-derived ureas that are potent antagonists or agonists of VR1, and which are useful for the treatment and prevention of inflammatory and other pain conditions in mammals. Approx. 120 compds. were prepared, and these plus addnl. compds. are claimed individually. Claims also relate to pharmaceutical compns., methods of treatment, and kits for treatment of a long list of diseases and conditions. For example, condensation of isoquinolin-5-ylcarbamic acid Ph ester with 1-benzyl-6-methoxy-1,2,3,4-tetrahydronaphthalen-2-ylamine HCl in DMSO in the presence of DIPEA at room temperature gave invention compound II. This compound inhibited binding of [3H]-RTX to recombinant human VR1 receptors in vitro with a Ki value of 3.37 nM. In functional expts., II blocked the activation of human recombinant VR1 elicited by agonists including low pH, PMA-induced PKC phosphorylation, anandamide, H2O2, and DTT; the potency was comparable to capsazepine. Compds. I also inhibited capsaicin-induced currents in dissociated rat DRG neurons. II potently antagonized capsaicin-induced contraction of isolated guinea pig bronchial rings, with an estimated pA2 of 8.0±0.02.

IT **628721-15-3P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of aminotetralin-derived ureas as vanilloid VR1 receptor modulators)
RN 628721-15-3 CAPLUS
CN Urea, N-[6-bromo-1,2,3,4-tetrahydro-1-(phenylmethyl)-2-naphthalenyl]-N'-8-isoquinolinyl- (9CI) (CA INDEX NAME)




RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

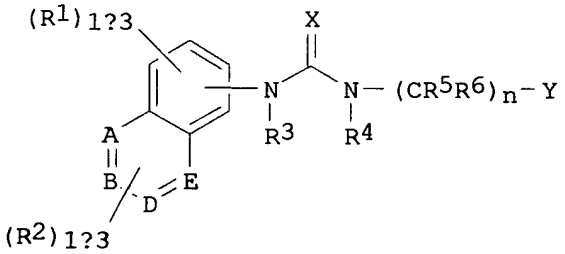
L5 ANSWER 8 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:777762 CAPLUS
DN 139:292162
TI Heteroaromatic ureas as vanilloid receptor (VR1) modulators, in particular antagonists, for treating pain and/or inflammation
IN Brown, Rebecca Elizabeth; Doughty, Victoria Alexandra; Hollingworth, Gregory John; Jones, A. Brian; Lindon, Matthew John; Moyes, Christopher Richard; Rogers, Lauren
PA Merck Sharp & Dohme Limited, UK
SO PCT Int. Appl., 110 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 2003080578 | A1 | 20031002 | WO 2003-GB1302 | 20030321 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2479150 | AA | 20031002 | CA 2003-2479150 | 20030321 |
| EP 1490340 | A1 | 20041229 | EP 2003-710014 | 20030321 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| US 2005107388 | A1 | 20050519 | US 2003-505358 | 20030321 |

| | | | | | |
|---|---|---|---|---|---|
| | JP 2005526798 | T2 | 20050908 | JP 2003-578333 | 20030321 |
| PRAI | GB 2002-6876 | A | 20020322 | | |
| | WO 2003-GB1302 | W | 20030321 | | |

OS MARPAT 139:292162

GI



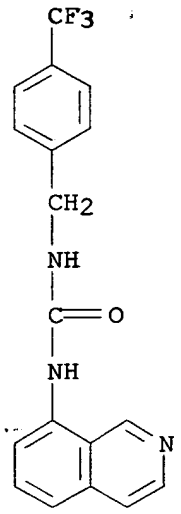
I

AB Title compds. I [wherein A, B, D, E are each C or N with the proviso that one or more are N; R1, R2 = independently H, halo, alk(enyl/ynyl), haloalkyl, hydroxyalkyl, cycloalkyl, cycloalkylalkyl, NH2 and derivs., CO2H and derivs., (un)substituted alkyl, alkoxy; R3, R4 = independently H, alk(en/yn)yl; R5, R6 = at each occurrence, independently H, alk(enyl/ynyl), alkoxy, acyloxy, carboxy and derivs., CONH2 and derivs., sulfonyl(alkyl/amino), aryl, hetero(aryl/cyclyl), (un)substituted alkyl; or CR5R6 = 3-6 carbocyclic membered ring; R7, R8 = at each occurrence, independently H, alk(en/yn)yl, cycloalkyl, fluoroalkyl; or NR7R8 = (un)substituted 4-7 heteroaliph. membered ring; X = O, S or =NCN; Y = aryl, heteroaryl, carbocyclyl, fused carbocyclyl group; n = 0, 1, 2, 3; and their pharmaceutically acceptable salts, N-oxides, and prodrugs] were prepared as vanilloid receptor (VR1) modulators, in particular antagonists, for treating conditions or diseases in which pain and/or inflammation predominates. For example, 1-isoquinolin-5-yl-3-(3-phenylpropyl)urea was prepared by reacting isoquinoline-5-carboxylic acid with diphenylphosphoryl azide in toluene at reflux for 1 h through a Curtius rearrangement, followed by addition of 3-phenylpropylamine and reflux for 18 h. I bound to the VR1 receptor with an IC50 < 1 μM, and in the majority of cases, < 200 nM. I are predominantly VR1 antagonists with a few of them VR1 partial antagonists and VR1 partial agonists. Thus, I and their pharmaceutical compns. are useful for treating pain and/or inflammation.

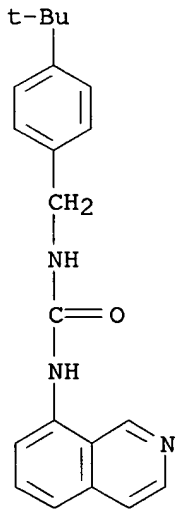
IT **581810-21-1P**, 1-Isoquinolin-8-yl-3-[4-(trifluoromethyl)benzyl]urea **608516-01-4P**, 1-(4-tert-Butylbenzyl)-3-isoquinolin-8-ylurea **608516-10-5P**, 1-Isoquinolin-8-yl-3-[3-[4-(trifluoromethyl)phenyl]propyl]urea **608516-12-7P**, 1-Isoquinolin-8-yl-3-[3-[3-(trifluoromethyl)phenyl]propyl]urea **608516-14-9P**, 1-Isoquinolin-8-yl-3-[4-(trifluoromethoxy)benzyl]urea **608516-43-4P**, 1-(3-Methoxyisoquinolin-8-yl)-3-[4-(trifluoromethyl)benzyl]urea **608516-49-0P**, 1-Isoquinolin-6-yl-3-[4-(trifluoromethyl)benzyl]urea **608516-50-3P**, 1-Isoquinolin-6-yl-3-[4-(trifluoromethoxy)benzyl]urea **608516-53-6P**, 1-(3-Methylisoquinolin-8-yl)-3-[4-(trifluoromethyl)benzyl]urea **608517-03-9P**, 1-Isoquinolin-7-yl-3-[4-(trifluoromethyl)benzyl]urea
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(Uses)
(VR1 receptor ligand; preparation of heteroarom. ureas as vanilloid receptor modulators for treating pain and inflammation)

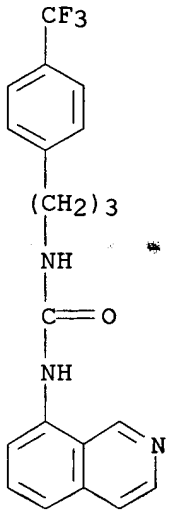
RN 581810-21-1 CAPLUS
CN Urea, N-8-isoquinolinyl-N'-[[4-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)



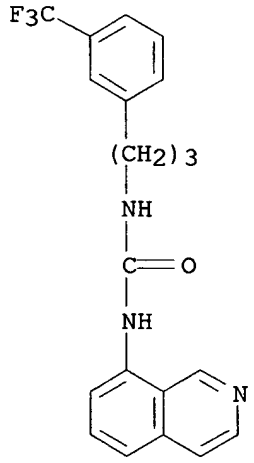

RN 608516-01-4 CAPLUS
CN Urea, N-[[4-(1,1-dimethylethyl)phenyl]methyl]-N'-8-isoquinolinyl- (9CI) (CA INDEX NAME)



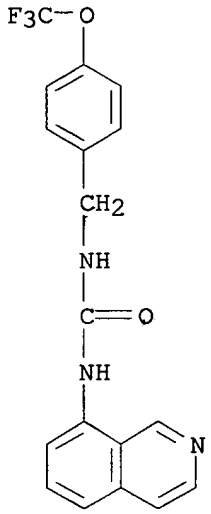

RN 608516-10-5 CAPLUS
CN Urea, N-8-isoquinolinyl-N'-[3-[4-(trifluoromethyl)phenyl]propyl]- (9CI) (CA INDEX NAME)



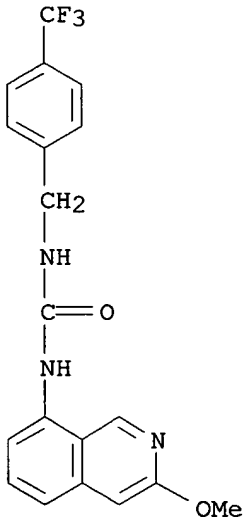
RN 608516-12-7 CAPLUS
CN Urea, N-8-isoquinolinyl-N'-[3-[3-(trifluoromethyl)phenyl]propyl]- (9CI) (CA INDEX NAME)



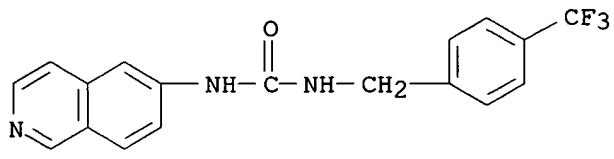
RN 608516-14-9 CAPLUS
CN Urea, N-8-isoquinolinyl-N'-[[4-(trifluoromethoxy)phenyl]methyl]- (9CI) (CA INDEX NAME)



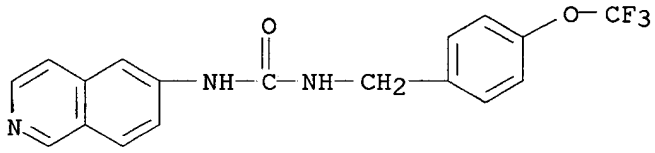
RN 608516-43-4 CAPLUS
CN Urea, N-(3-methoxy-8-isoquinolinyl)-N'-[[4-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)



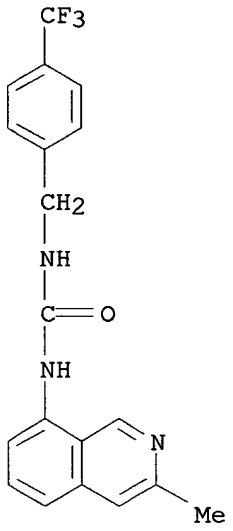
RN 608516-49-0 CAPLUS
CN Urea, N-6-isoquinolinyl-N'-[[4-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)



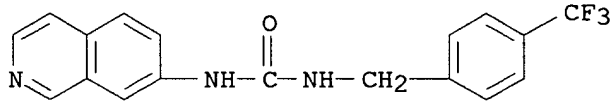
RN 608516-50-3 CAPLUS
CN Urea, N-6-isoquinolinyl-N'-[[4-(trifluoromethoxy)phenyl]methyl]- (9CI) (CA INDEX NAME)



RN 608516-53-6 CAPLUS
CN Urea, N-(3-methyl-8-isoquinolinyl)-N'-[[4-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)



RN 608517-03-9 CAPLUS
CN Urea, N-7-isoquinolinyl-N'-[[4-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)



RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 9 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:656417 CAPLUS
DN 139:197383
TI Preparation of fused azabicyclic compounds that inhibit vanilloid receptor subtype 1 (VR1)
IN Lee, Chih-Hung; Bayburt, Erol K.; Didomenico, Stanley; Drizin, Irene;

Gomtsyan, Arthur R.; Koenig, John R.; Perner, Richard J.; Schmidt, Robert G.; Turner, Sean C.; White, Tammie K.; Zheng, Guo Zhu

PA USA

SO U.S. Pat. Appl. Publ., 79 pp.
CODEN: USXXCO

DT Patent

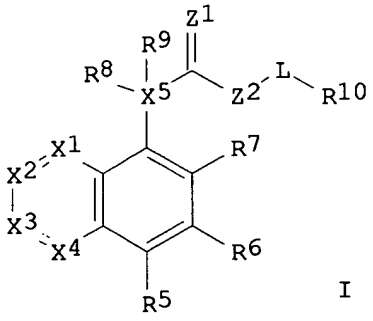
LA English

FAN.CNT 3

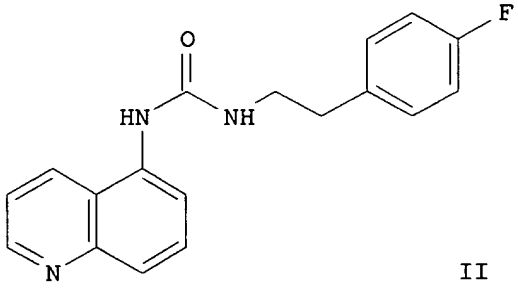
| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | US 2003158198 | A1 | 20030821 | US 2003-364210 | 20030211 |
| | CA 2476936 | AA | 20030828 | CA 2003-2476936 | 20030211 |
| | WO 2003070247 | A1 | 20030828 | WO 2003-US4187 | 20030211 |
| | W: CA, JP, MX | | | | |
| | RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR | | | | |
| | EP 1478363 | A1 | 20041124 | EP 2003-716014 | 20030211 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| | US 2004157849 | A1 | 20040812 | US 2003-634678 | 20030805 |
| | US 6933311 | B2 | 20050823 | | |
| | US 2004209884 | A1 | 20041021 | US 2004-842311 | 20040510 |
| PRAI | US 2002-358220P | P | 20020220 | | |
| | US 2002-79324 | A | 20020220 | | |
| | US 2003-364210 | A | 20030211 | | |
| | WO 2003-US4187 | W | 20030211 | | |

OS MARPAT 139:197383

GI



I

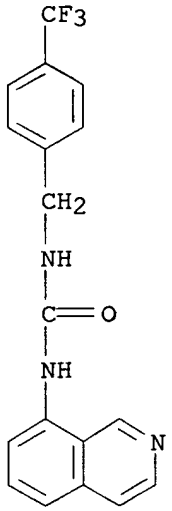


II

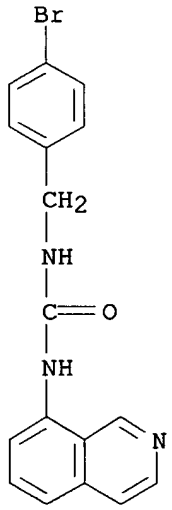
AB Compds. of formula I [X1-X5 = (substituted) N, (substituted) CH; Z1 = O, NH, S; Z2 = bond, NH, O; L = alkylene, cycloalkylene, piperazinediyl, etc.; R5-R9 = H, alkyl, alkenyl, alkoxy, carboxy, cycloalkyl, formyl, mercapto, etc.; R10 = H, aryl, cycloalkyl, heterocyclyl] are prepared as vanilloid receptor subtype 1 (VR1) antagonists that are useful in treating pain, inflammatory thermal hyperalgesia, urinary incontinence and bladder overactivity. Thus, II was prepared from 5-aminoisoquinoline and 2-(3-fluorophenyl)ethylamine. The prepared compds. were found to be antagonists of VR1 with IC50 of.1 nM to 1000 nM.

IT **581810-21-1P 581810-22-2P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of fused azabicyclic compds. as vanilloid receptor 1

inhibitors)
RN 581810-21-1 CAPLUS
CN Urea, N-8-isoquinolinyl-N'-[[4-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)



RN 581810-22-2 CAPLUS
CN Urea, N-[(4-bromophenyl)methyl]-N'-8-isoquinolinyl- (9CI) (CA INDEX NAME)

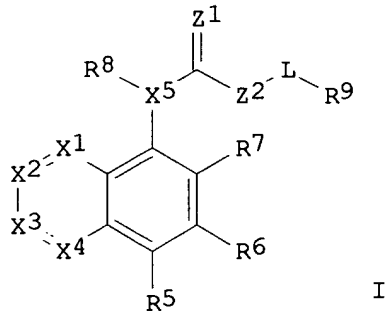


L5 ANSWER 10 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:656416 CAPLUS
DN 139:197382
TI Preparation of isoquinolines, indoles, and related compounds as antagonists of vanilloid receptor subtype 1 (VR1).
IN Lee, Chih-Hung; Bayburt, Erol K.; Didomenico, Stanley; Drizin, Irene; Gomtsyan, Arthur R.; Koenig, John R.; Perner, Richard J.; Schmidt, Robert

G.; Turner, Sean C.; White, Tammie K.; Zheng, Guo Zhu
PA USA
SO U.S. Pat. Appl. Publ., 38 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 3

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | US 2003158188 | A1 | 20030821 | US 2002-79324 | 20020220 |
| | CA 2476936 | AA | 20030828 | CA 2003-2476936 | 20030211 |
| | WO 2003070247 | A1 | 20030828 | WO 2003-US4187 | 20030211 |
| | W: CA, JP, MX | | | | |
| | RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR | | | | |
| | EP 1478363 | A1 | 20041124 | EP 2003-716014 | 20030211 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| PRAI | US 2002-79324 | A | 20020220 | | |
| | US 2003-364210 | A | 20030211 | | |
| | WO 2003-US4187 | W | 20030211 | | |

OS MARPAT 139:197382
GI



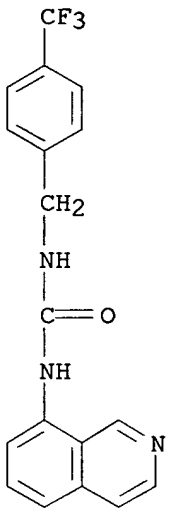
I

AB Title compds. [I; X1 = N, CR1; X2 = N, CR2; X3 = N, NR3, CR3; X4 = null, N, CR4; X5 = N, CH2; Z1 = O, NH, S; Z2 = NH, O; L = piperazinylene, alkenylene, alkylene, alkynylene, cycloalkylene, (CH2)mO(CH2)n, NHO, NHNH; m, n = 1-6; R1, R3, R5, R6, R7 = H, alkenyl, alkoxy, alkoxyalkoxy, alkoxyalkyl, alkoxycarbonyl, alkoxycarbonylalkyl, A, ACO, ACOA, ACO2, AS, alkynyl, CO2H, ACO2H, cyano, cyanoalkyl, cycloalkyl, cycloalkylalkyl, ethylenedioxy, CHO, ACHO, haloalkoxy, haloalkyl, haloalkylthio, halo, OH, HOA, methylenedioxy, SH, ASH, NO2, (CF3)2(HO)C, NRASO2RB, SO2ORA, SO2RB, NZAZB, (NZAZB)A, (NZAZB)CO, (NZAZB)COA, (NZAZB)SO2; ZA, ZB = H, A, ACO, CHO, aryl, aralkyl; R2, R4 = H, alkenyl, AO, alkoxyalkoxy, AOA, AO2C, AO2CA, A, ACO, ACOA, ACO2, AS, alkynyl, CO2H, carboxyalkyl, cyano, cyanoalkyl, cycloalkyl, cycloalkylalkyl, ethylenedioxy, CHO, ACHO, haloalkoxy, haloalkyl, haloalkylthio, halo, OH, HOA, methylenedioxy, SH, HSA, NO2, (CF3)2(HO)C, NRAS(O)2RB, SO2ORA, SO2RB, NZAZB, (NZAZB)alkyl, (NZAZB)ACO, (NZAZB)CO, (NZAZB)COA, (NZAZB)SO2, (NZAZB)C(:NH), (NZAZB)C(:NCN)NH, (NZAZB)C(:NH)NH; RA = H, A; RB = A, aryl, aralkyl; R8 = null, H, A; R9 = H, aryl, heterocycle; A = alkyl; dotted line = optional

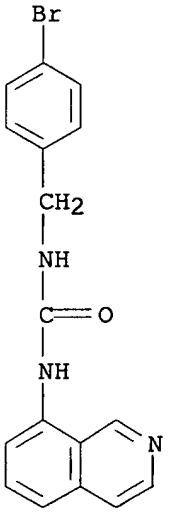
double bond], were prepared for treating pain, inflammatory thermal hyperalgesia, urinary incontinence and bladder overactivity (no data). Thus, 2,2,2-trichloro-N-isoquinolin-5-ylacetamide, (preparation given) DBU, and 2-(3-fluorophenyl)ethylamine in acetonitrile were refluxed for 10 h to give 65% N-[2-(3-fluorophenyl)ethyl]-N'-isoquinolin-5-ylurea.

IT **581810-21-1P 581810-22-2P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(claimed compound; preparation of isoquinolines, indoles, and related compds.
as antagonists of vanilloid receptor subtype 1)

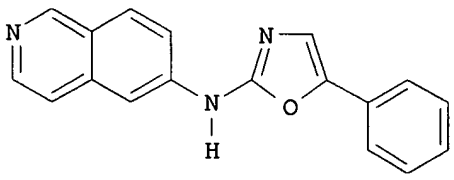
RN 581810-21-1 CAPLUS
CN Urea, N-8-isoquinolinyl-N'-[[4-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)



RN 581810-22-2 CAPLUS
CN Urea, N-[(4-bromophenyl)methyl]-N'-8-isoquinolinyl- (9CI) (CA INDEX NAME)



L5 ANSWER 11 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:236040 CAPLUS
DN 139:133492
TI Identification of novel and potent isoquinoline aminooxazole-based IMPDH inhibitors
AU Chen, Ping; Norris, Derek; Haslow, Kristin D.; Murali Dhar, T. G.; Pitts, William J.; Watterson, Scott H.; Cheney, Daniel L.; Bassolino, Donna A.; Fleener, Catherine A.; Rouleau, Katherine A.; Hollenbaugh, Diane L.; Townsend, Robert M.; Barrish, Joel C.; Iwanowicz, Edwin J.
CS Discovery Chemistry, Bristol-Myers Squibb Pharmaceutical Research Institute, Princeton, NJ, 08543, USA
SO Bioorganic & Medicinal Chemistry Letters (2003), 13(7), 1345-1348
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science B.V.
DT Journal
LA English
OS CASREACT 139:133492
GI



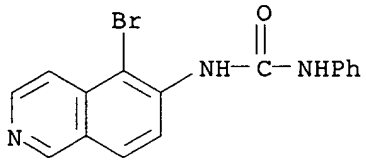
II

AB Screening of our inhouse compound collection led to the discovery of 5-bromo-6-aminoisoquinoline (I) as a weak inhibitor of IMPDH. Subsequent optimization of I afforded a series of novel 2-isoquinolinoaminooxazole-based inhibitors, e.g., II, with single-digit nanomolar potency against the enzyme.

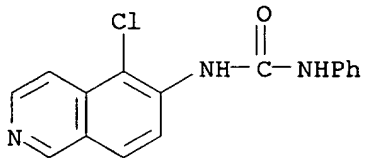
IT **566944-08-9P 566944-09-0P 566944-10-3P**
**566944-11-4P 566944-12-5P 566944-13-6P**

**566944-14-7P 566944-15-8P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation, IMPDH inhibition, and structure-activity relationships of isoquinolinylureas via addition of aminoisoquinolines to aryl isocyanates)

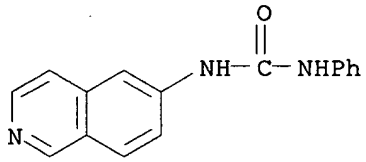
RN 566944-08-9 CAPLUS
CN Urea, N-(5-bromo-6-isoquinolinyl)-N'-phenyl- (9CI) (CA INDEX NAME)



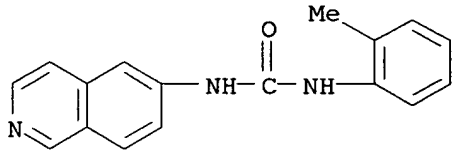

RN 566944-09-0 CAPLUS
CN Urea, N-(5-chloro-6-isoquinolinyl)-N'-phenyl- (9CI) (CA INDEX NAME)



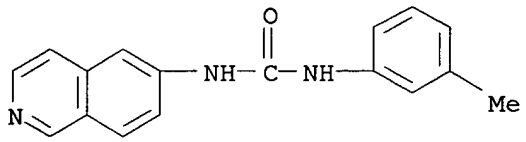

RN 566944-10-3 CAPLUS
CN Urea, N-6-isoquinolinyl-N'-phenyl- (9CI) (CA INDEX NAME)



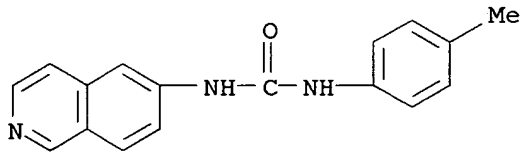

RN 566944-11-4 CAPLUS
CN Urea, N-6-isoquinolinyl-N'-(2-methylphenyl)- (9CI) (CA INDEX NAME)



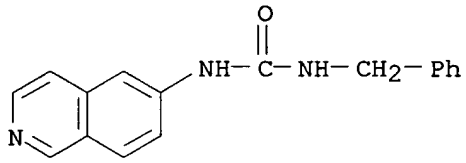

RN 566944-12-5 CAPLUS
CN Urea, N-6-isoquinolinyl-N'-(3-methylphenyl)- (9CI) (CA INDEX NAME)



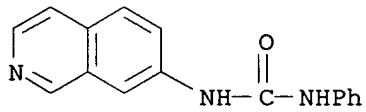
RN 566944-13-6 CAPLUS
CN Urea, N-6-isoquinolinyl-N'-(4-methylphenyl)- (9CI) (CA INDEX NAME)



RN 566944-14-7 CAPLUS
CN Urea, N-6-isoquinolinyl-N'-(phenylmethyl)- (9CI) (CA INDEX NAME)



RN 566944-15-8 CAPLUS
CN Urea, N-7-isoquinolinyl-N'-phenyl- (9CI) (CA INDEX NAME)



RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

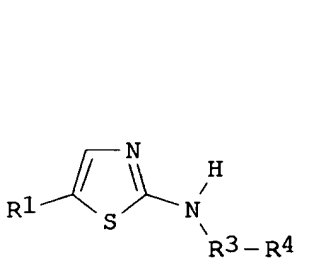
L5 ANSWER 12 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2002:866687 CAPLUS
DN 137:353013
TI Thiazole derivatives and their use as cdk inhibitors, including combinations and pharmaceutical compositions
IN Cooper, Christopher Blair; Helal, Christopher John; Sanner, Mark Allen
PA Pfizer Products Inc., USA
SO Eur. Pat. Appl., 32 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|

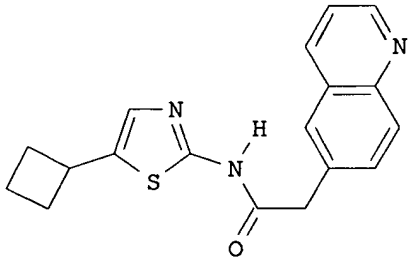
| | | | | | |
|---|---|---|---|---|---|
| PI | EP 1256578 | A1 | 20021113 | EP 2002-253106 | 20020502 |
| | EP 1256578 | B1 | 20060111 | | |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| | JP 2002338556 | A2 | 20021127 | JP 2002-132275 | 20020508 |
| | CA 2385692 | AA | 20021111 | CA 2002-2385692 | 20020509 |
| | BR 2002001691 | A | 20030311 | BR 2002-1691 | 20020513 |
| | US 2003078252 | A1 | 20030424 | US 2002-144403 | 20020513 |
| | US 6720427 | B2 | 20040413 | | |
| | US 2004192746 | A1 | 20040930 | US 2004-818876 | 20040405 |
| PRAI | US 2001-290466P | P | 20010511 | | |
| | US 2002-144403 | A1 | 20020513 | | |

OS MARPAT 137:353013

GI



I

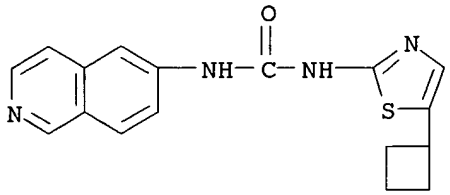


II

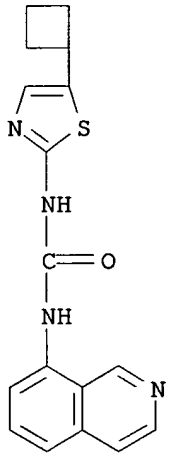
AB The invention provides compds. thiazole derivs. I [wherein: R1 = (un)substituted alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, heterocycloalkyl, bicycloalkyl, bicycloalkenyl, heterobicycloalkyl, aryl, heteroaryl, or amino including cyclic amino; R3 = (un)substituted CONH, COO, CO(CH2)n, (CH2)n; R4 = as given for R1 except amino; n = 0-3; including pharmaceutically acceptable salts]. I are inhibitors of cyclin-dependent protein kinases (cdk), particularly cdk5, cdk2, and GSK-3. Pharmaceutical compns. and methods comprising compds. I are described, particularly for treating diseases and conditions comprising abnormal cell growth, such as cancer, and neurodegenerative diseases and conditions and those affected by dopamine neurotransmission. Also described are pharmaceutical compns. and methods comprising compds. I for treating or improving the following: male fertility and sperm motility problems, diabetes mellitus, impaired glucose tolerance, metabolic syndrome or syndrome X, polycystic ovary syndrome, adipogenesis and obesity, myogenesis and frailty (for example age-related decline in phys. performance), acute sarcopenia (for example, muscle atrophy and/or cachexia associated with burns, bed rest, limb immobilization, or major thoracic, abdominal, and/or orthopedic surgery), sepsis, hair loss, hair thinning, balding, and immunodeficiency. Approx. 90 specific compds. I are claimed, and the prepns. of 5 of these and several intermediates are exemplified. For instance, 2-aminothiazole was lithiated and silylated, then re-lithiated and treated with cyclobutanone to give 1-(2-aminothiazol-5-yl)cyclobutanol. This alc. was hydrogenated to give 5-cyclobutylthiazol-2-ylamine, which was coupled with 6-quinolylacetic acid using T3P (1-propanephosphonic acid cyclic trimeric anhydride), to give title compound II. The 5 exemplified compds. all had IC50 values of < 50 μM for inhibiting cdk5, cdk2, and GSK-3β in vitro.

IT **474460-64-5P**, 1-(5-Cyclobutylthiazol-2-yl)-3-isoquinolin-6-ylurea
**474461-02-4P**, 1-(5-Cyclobutylthiazol-2-yl)-3-isoquinolin-8-ylurea

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of thiazole derivs. as cdk inhibitors)
RN 474460-64-5 CAPLUS
CN Urea, N-(5-cyclobutyl-2-thiazolyl)-N'-6-isoquinolinyl- (9CI) (CA INDEX NAME)



RN 474461-02-4 CAPLUS
CN Urea, N-(5-cyclobutyl-2-thiazolyl)-N'-8-isoquinolinyl- (9CI) (CA INDEX NAME)



RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 13 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2002:107923 CAPLUS
DN 136:151166
TI Preparation of imidazoisoquinolinones as inhibitors of tyrosine kinases
IN Snow, Roger John; Cardozo, Mario; Goldberg, Daniel; Hammach, Abdelhakim; Morwick, Tina; Moss, Neil; Patel, Usha R.; Prokopowicz, Anthony S.; Takahashi, Hidenori; Tschantz, Matt Aaron; Wang, Xiao-Jun
PA Boehringer Ingelheim Pharmaceuticals, Inc., USA
SO U.S. Pat. Appl. Publ., 62 pp., Cont.-in-part of U.S. Ser. No. 679,156.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2
PATENT NO. KIND DATE APPLICATION NO. DATE

| | | | | | |
|---|---|---|---|---|---|
| PI | US 2002016460 | A1 | 20020207 | US 2001-921509 | 20010802 |
| | US 6506769 | B2 | 20030114 | | |
| | US 2003166929 | A1 | 20030904 | US 2002-292026 | 20021112 |
| | US 6770639 | B2 | 20040803 | | |
| PRAI | US 1999-157922P | P | 19991006 | | |
| | US 2000-679156 | A2 | 20001005 | | |
| | US 2001-921509 | A3 | 20010802 | | |

OS CASREACT 136:151166; MARPAT 136:151166

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

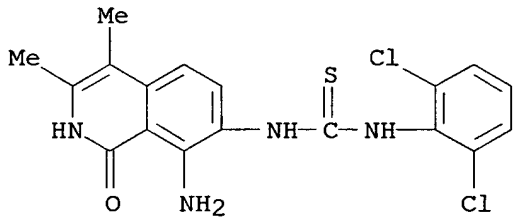
AB The title compds. [I; Ar1 = (un)substituted (non)aromatic carbocyclyl, heteroaryl, heterocyclyl; X = NH, N(alkyl), O, etc.; Y = NR15, S, O; Ra = H, alkyl, alkenyl, etc.; R4 and R5 together with the atoms to which they are attached = II, III (wherein R6 = alkyl, H; R7 = alkyl, H; R8 = H, alkyl, etc.; R9 = H, CN, etc.)], useful as inhibitors of certain protein tyrosine kinases and are thus useful for treating diseases associated with such kinases, for example, diseases resulting from inappropriate cell proliferation, which include autoimmune diseases, chronic inflammatory diseases, allergic diseases, transplant rejection and cancer, as well as conditions resulting from cerebral ischemia, such as stroke, were prepared All exemplified compds. I were evaluated in the tyrosine kinase assay using a kinase such a p56lck and were found to have IC50's less than 10 μM. Methods of preparation are claimed and 29 example prepns. are included. E.g., a multi-step synthesis of the imidazoisoquinolinedione IV was given. Claimed methods include: a method of making I wherein X is N-R15 and Ar1, R4, R5, R15and Ra are as defined in claim 1, said process comprising: (a) reacting a phenylenediamine with Ar1NCS in a suitable solvent at about ambient to reflux temperature for .apprx.3 to 24 h to provide a possibly substituted N-(o-aminophenyl)thiourea (b) reacting this product with a suitable activating agent chosen from 1,3-dicyclohexylcarbodiimide (DCC) and mercuric oxide in a suitable solvent at about ambient to reflux temperature Also, a method of making I wherein X is S, Y is NH and Ar1, R4, R5 and Ra are as defined in claim 1, said process comprising: (a) reacting an aniline with Ar1NCS in a suitable solvent at about ambient to reflux temperature for .apprx.3 to 24 h to form a thiourea; (b) reacting this product under cyclizing conditions in a suitable solvent at about reflux temperature Also, a method of making V wherein R15, R8 and R9 are as described in claim 1, said method comprising: (a) reacting 2,6-dichloro-3-nitrobenzonitrile with NHR15 in a suitable solvent optionally in a pressure flask and at .apprx.0 to 80°, to provide 2-R15NH-3-nitro-6-chlorobenzonitriles, and subsequently reacting these compds. with ketoester R9C(O)CHR8CO2Et in the presence of a suitable base in a suitable solvent, at about ambient temperature to form 2-NC-3-R15NH-4-O2NC6H2CR8(C(O)R9)CO2Et (b) hydrolyzing this product by reacting with aqueous acid, and cyclizing at about reflux temperature; followed by reducing the cyclized product in a suitable solvent. Also, a method of making VI wherein Ra, R8, R9 and Ar1 are as described in claim 1, said method comprising: (a) reacting a phenylenediamine with Br2 in a suitable solvent at ambient temperature to provide a brominated ring product; (b) reacting this product with Ar1NCS in a suitable solvent at about ambient to reflux temperature for .apprx.3 to 24 h and subsequently reacting the

product with a suitable activating agent chosen from DCC and mercuric oxide in a suitable solvent at about ambient to reflux temperature to form VI with Ra = Br; (c) cross-coupling to introduce Ra in place of Br in the presence of a suitable catalyst in a suitable solvent at .apprx.100°.

IT **333458-37-0P**, Thiourea, N-(8-amino-1,2-dihydro-3,4-dimethyl-1-oxo-7-isoquinolinyl)-N'-(2,6-dichlorophenyl)- **333458-53-0P**, Thiourea, N-(2,6-dichlorophenyl)-N'-(1,2-dihydro-3,4-dimethyl-1-oxo-7-isoquinolinyl)-
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of imidazoisoquinolinones as inhibitors of tyrosine kinases)

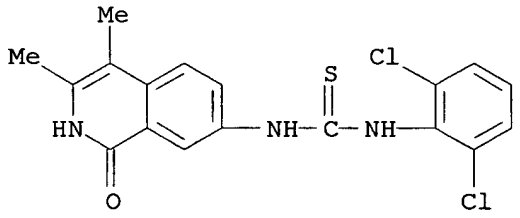
RN 333458-37-0 CAPLUS

CN Thiourea, N-(8-amino-1,2-dihydro-3,4-dimethyl-1-oxo-7-isoquinolinyl)-N'-(2,6-dichlorophenyl)- (9CI) (CA INDEX NAME)



RN 333458-53-0 CAPLUS

CN Thiourea, N-(2,6-dichlorophenyl)-N'-(1,2-dihydro-3,4-dimethyl-1-oxo-7-isoquinolinyl)- (9CI) (CA INDEX NAME)



L5 ANSWER 14 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2001:265421 CAPLUS

DN 134:280844

TI Preparation of imidazoisoquinolinones as inhibitors of tyrosine kinases

IN Snow, Roger John; Cardozo, Mario Gustavo; Goldberg, Daniel; Hammach, Abdelhakim; Morwick, Tina; Moss, Neil; Patel, Usha R.; Prokopowicz, Anthony S., III; Takahashi, Hidenori; Tschantz, Matt Aaron; Wang, Xiao-jun

PA Boehringer Ingelheim Pharmaceuticals, Inc., USA

SO PCT Int. Appl., 169 pp.
CODEN: PIXXD2

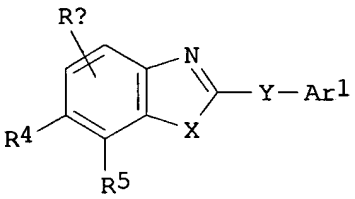
DT Patent

LA English

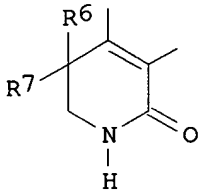
FAN.CNT 2

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|

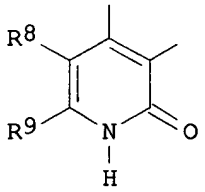
PI WO 2001025238 A2 20010412 WO 2000-US27444 20001005
WO 2001025238 A3 20011025
W: CA, JP, MX
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
CA 2384378 AA 20010412 CA 2000-2384378 20001005
EP 1222187 A2 20020717 EP 2000-968713 20001005
EP 1222187 B1 20040922
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY
JP 2003527328 T2 20030916 JP 2001-528182 20001005
AT 277044 E 20041015 AT 2000-968713 20001005
ES 2225231 T3 20050316 ES 2000-968713 20001005
PRAI US 1999-157922P P 19991006
WO 2000-US27444 W 20001005
OS MARPAT 134:280844
GI



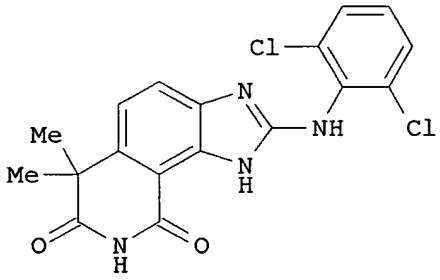

I




II




III



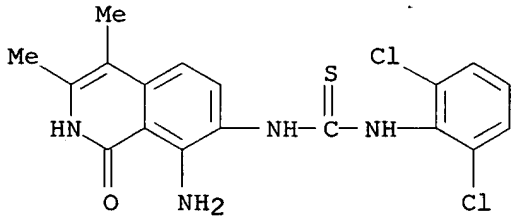

IV

AB The title compds. [I; Ar1 = (un)substituted (non)aromatic carbocyclyl, heteroaryl, heterocyclyl; X = NH, N(alkyl), O, etc.; Y = NR15, S, O; Ra = H, alkyl, alkenyl, etc.; R4 and R5 together with the atoms to which they are attached = II, III (wherein R6 = alkyl, H; R7 = alkyl, H; R8 = H, alkyl, etc.; R9 = H, CN, etc.)], useful as inhibitors of certain protein tyrosine kinases and are thus useful for treating diseases associated with such kinases, for example, diseases resulting from inappropriate cell proliferation, which include autoimmune diseases, chronic inflammatory diseases, allergic diseases, transplant rejection and cancer, were prepared E.g., a multi-step synthesis of the imidazoisoquinolinedione IV was given. All exemplified compds. I were evaluated in the tyrosine kinase assay using a kinase such a p56lck and were found to have IC50's less than 10

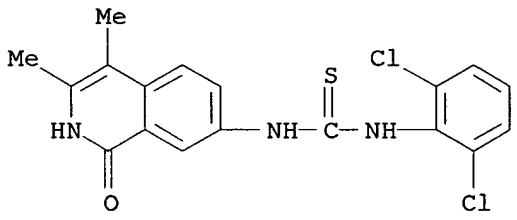
μM.

IT **333458-37-0P 333458-53-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of imidazoisoquinolinones as inhibitors of tyrosine kinases)

RN 333458-37-0 CAPLUS
CN Thiourea, N-(8-amino-1,2-dihydro-3,4-dimethyl-1-oxo-7-isoquinolinyl)-N'-(2,6-dichlorophenyl)- (9CI) (CA INDEX NAME)



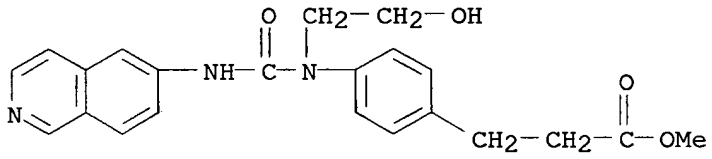
RN 333458-53-0 CAPLUS
CN Thiourea, N-(2,6-dichlorophenyl)-N'-(1,2-dihydro-3,4-dimethyl-1-oxo-7-isoquinolinyl)- (9CI) (CA INDEX NAME)



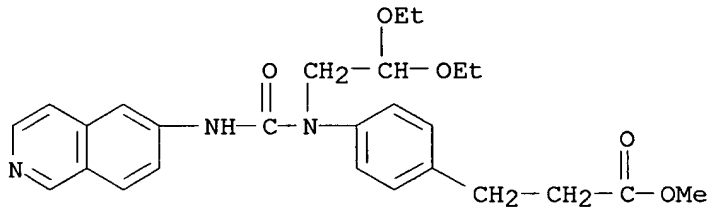
L5 ANSWER 15 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1995:550906 CAPLUS
DN 122:314547
TI Preparation of urea residue-substituted heterocyclic compounds with antithrombotic, antineoplastic and blood platelet-aggregation inhibition activities
IN Himmelsbach, Frank; Pieper, Helmut; Austel, Volkhard; Linz, Guenter; Guth, Brian; Mueller, Thomas; Weisenberger, Johannes
PA Dr. Karl Thomae GmbH, Germany
SO Eur. Pat. Appl., 81 pp.
CODEN: EPXXDW
DT Patent
LA German
FAN.CNT 3

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI EP 612741 | A1 | 19940831 | EP 1994-102557 | 19940221 |
| EP 612741 | B1 | 19980610 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE | | | | |
| DE 4305388 | A1 | 19940825 | DE 1993-4305388 | 19930222 |
| DE 4332168 | A1 | 19950323 | DE 1993-4332168 | 19930922 |
| EE 3397 | B1 | 20010416 | EE 1994-311 | 19941123 |

PRAI DE 1993-4305388 A 19930222
DE 1993-4332168 A 19930922
OS MARPAT 122:314547
AB The title compds., which contain urea-like moieties, often in the form of divalent imidazolidinone groups, which demonstrate a combination of antithrombotic, antineoplastic (no data), and blood platelet-aggregation inhibition activities, are prepared and pharmaceutical dosage forms containing them presented. Thus, 1-[4-(2-carboxyethyl)phenyl]-3-(1,2,3,4-tetrahydroisoquinolin-6-yl)imidazolidin-2-one was prepared and demonstrated ED50 for blood platelet aggregation inhibition of 40 nM.
IT **158726-22-8P 158726-36-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of urea residue-substituted heterocyclic compds. with antithrombotic, antineoplastic and blood platelet-aggregation inhibition activities)
RN 158726-22-8 CAPLUS
CN Benzenepropanoic acid, 4-[(2-hydroxyethyl)[(6-isoquinolinylamino)carbonyl]amino]-, methyl ester (9CI) (CA INDEX NAME)

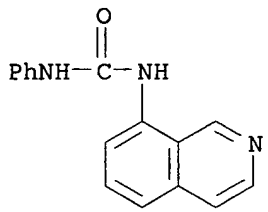


RN 158726-36-4 CAPLUS
CN Benzenepropanoic acid, 4-[(2,2-diethoxyethyl)[(6-isoquinolinylamino)carbonyl]amino]-, methyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 16 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1995:95816 CAPLUS
DN 122:132936
TI Phenylisoquinolinyl derivatives of urea
AU Nowak, Krystyna; Poradowska, Henryka
CS Pol.
SO Czasopismo Techniczne (Krakow) (1992), 89(1), 7-12
CODEN: CZTEAY; ISSN: 0011-4561
DT Journal
LA Polish
OS CASREACT 122:132936
AB Adding PhNCO in dry PhMe to 1-, 4-, 5- or 8-aminoisoquinoline solution gave the corresponding isoquinolylphenylureas quant. These products are potential plant-growth stimulants.

IT **119612-65-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of isoquinolylphenylureas by addition reaction of aminoisoquinolines with Ph isocyanate)
RN 119612-65-6 CAPLUS
CN Urea, N-8-isoquinolinyl-N'-phenyl- (9CI) (CA INDEX NAME)



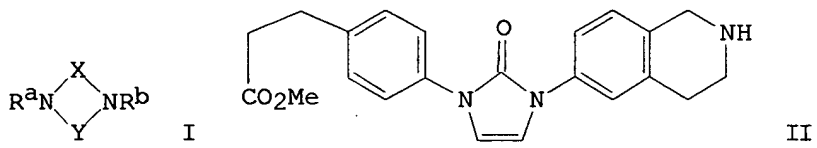
L5 ANSWER 17 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1994:680641 CAPLUS
DN 121:280641
TI Preparation of N-arylazolones as tissue aggregation inhibitors
IN Himmelsbach, Frank; Pieper, Helmut; Austel, Volkhard; Linz, Guenter; Guth, Brian; Mueller, Thomas; Weisenberger, Johannes
PA Dr. Karl Thomae GmbH, Germany
SO Ger. Offen., 46 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 3

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | DE 4305388 | A1 | 19940825 | DE 1993-4305388 | 19930222 |
| | DE 4332168 | A1 | 19950323 | DE 1993-4332168 | 19930922 |
| | TW 384286 | B | 20000311 | TW 1994-83101259 | 19940217 |
| | CA 2116068 | AA | 19940823 | CA 1994-2116068 | 19940221 |
| | FI 9400806 | A | 19940823 | FI 1994-806 | 19940221 |
| | NO 9400595 | A | 19940823 | NO 1994-595 | 19940221 |
| | AU 9456324 | A1 | 19940825 | AU 1994-56324 | 19940221 |
| | AU 673875 | B2 | 19961128 | | |
| | EP 612741 | A1 | 19940831 | EP 1994-102557 | 19940221 |
| | EP 612741 | B1 | 19980610 | | |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE | | | | |
| | JP 06256343 | A2 | 19940913 | JP 1994-22727 | 19940221 |
| | JP 3545446 | B2 | 20040721 | | |
| | ZA 9401159 | A | 19950821 | ZA 1994-1159 | 19940221 |
| | HU 70768 | A2 | 19951030 | HU 1994-493 | 19940221 |
| | AT 167185 | E | 19980615 | AT 1994-102557 | 19940221 |
| | ES 2118992 | T3 | 19981001 | ES 1994-102557 | 19940221 |
| | RU 2126002 | C1 | 19990210 | RU 1994-6007 | 19940221 |
| | PL 178215 | B1 | 20000331 | PL 1994-302302 | 19940221 |
| | CN 1099755 | A | 19950308 | CN 1994-102252 | 19940222 |
| | CN 1048490 | B | 20000119 | | |
| | US 5519036 | A | 19960521 | US 1994-200125 | 19940222 |
| | IL 108733 | A1 | 19980104 | IL 1994-108733 | 19940222 |
| | US 5612335 | A | 19970318 | US 1995-434136 | 19950502 |
| | US 5827849 | A | 19981027 | US 1996-768365 | 19961217 |
| PRAI | DE 1993-4305388 | A | 19930222 | | |

| | | | |
|---|---|---|---|
| | DE 1993-4332168 | A | 19930922 |
| | US 1994-200125 | A3 | 19940222 |
| | US 1995-434136 | A3 | 19950502 |
| | DE 1996-19624069 | A | 19960617 |

OS MARPAT 121:280641

GI



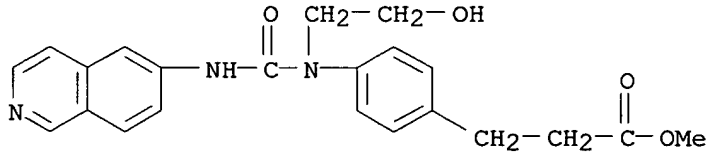
I II

AB Title compds. [I; Ra,Rb = AB; A = benzene ring-attached benzanellated N-containing heterocyclyl; B = bond, alk(en)ylene, arylene, etc.; X = (N-substituted) C(:NH), CO, SO1-2, etc.; Y = alk(en)ylene, 1,2-cycloalk(en)ylene, 1,2-phenylene, etc.] were prepared Thus, 4-(MeO2CH2CH2C)C6H4NHCH2CH2OH and 6-aminoisoquinoline were condensed with N,N'-carbonyldiimidazole to give 4-(MeO2CH2CH2C)C6H4NH(CH2CH2OH)CONHR (R = 6-isoquinolinyl). 4-(MeO2CH2CH2C)C6H4NH[CH2CH2(OEt)2]CONHR (R = unchanged) was cyclized and the product hydrogenated in HOAc to give phenylisoquinolinylimidazolone II.HOAc which had IC50 of 40nM against collagen-induced platelet aggregation in vitro.

IT **158726-22-8P 158726-36-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of N-arylazolones as tissue aggregation inhibitors)

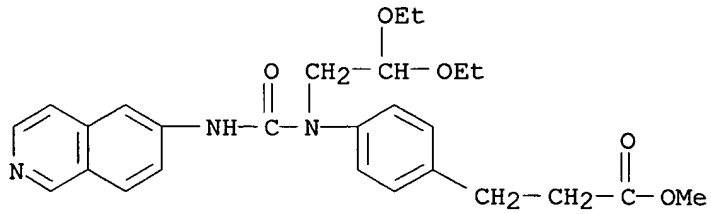
RN 158726-22-8 CAPLUS

CN Benzenepropanoic acid, 4-[(2-hydroxyethyl)[(6-isoquinolinylamino)carbonyl]amino]-, methyl ester (9CI) (CA INDEX NAME)



RN 158726-36-4 CAPLUS

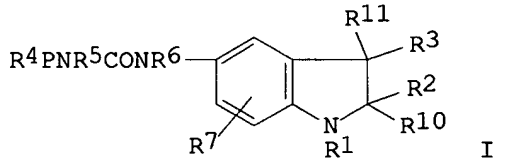
CN Benzenepropanoic acid, 4-[(2,2-diethoxyethyl)[(6-isoquinolinylamino)carbonyl]amino]-, methyl ester (9CI) (CA INDEX NAME)



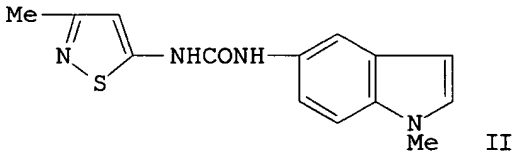
L5 ANSWER 18 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1994:77171 CAPLUS
DN 120:77171
TI Preparation of indolylurea derivatives as antagonists
IN Forbes, Ian Thomson; Martin, Roger Thomas; Jones, Graham Elgin
PA SmithKline Beecham PLC, UK
SO PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 9318028 | A1 | 19930916 | WO 1993-GB449 | 19930304 |
| | W: AU, CA, JP, KR, NZ, US | | | | |
| | RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| | AU 9336411 | A1 | 19931005 | AU 1993-36411 | 19930304 |
| | EP 630373 | A1 | 19941228 | EP 1993-905507 | 19930304 |
| | R: BE, CH, DE, FR, GB, IT, LI, NL | | | | |
| | JP 07504429 | T2 | 19950518 | JP 1993-515449 | 19930304 |
| | ZA 9301713 | A | 19940922 | ZA 1993-1713 | 19930310 |
| | US 5508288 | A | 19960416 | US 1994-295694 | 19940830 |
| PRAI | GB 1992-5415 | A | 19920312 | | |
| | GB 1992-5416 | A | 19920312 | | |
| | GB 1992-5422 | A | 19920312 | | |
| | GB 1992-5442 | A | 19920312 | | |
| | WO 1993-GB449 | A | 19930304 | | |

OS MARPAT 120:77171
GI




I

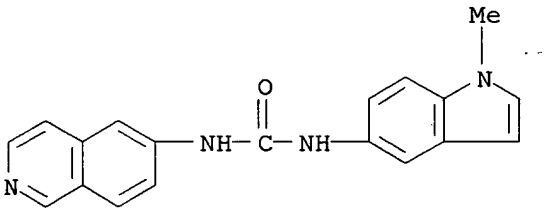



II

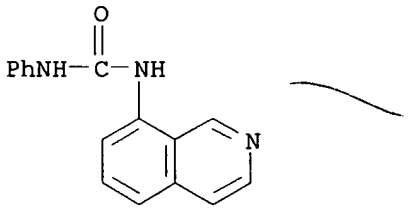
AB Title compds. I (P = quinolinyl, isoquinolyl, 5,6-membered heterocyclyl; R1 = H, C1-6 alkyl; R2, R3, R10, R11 = C2-6 alkylene; R4 = H, C1-6 alkyl, halo, R8R9N, R12O, R12O2C wherein R8, R9, R12 = H, C1-6 alkyl; R5, R6 = H, C1-6 alkyl; R7 = H, C1-6 alkyl, C1-6 alkoxy, halo; etc.) or a salt thereof, are prepared to NaH was added 5-amino-3-methylbisthiazole-HCl followed by N-(1-methyl-5-indolyl)carbamate (preparation given) to give the title compound II. The affinity of II for 5-HT1C binding site by assessing its ability to displace [3H]-mesulergine from 5-HT1C binding sites was shown by pA2 as 7.9.

IT **152239-58-2P**

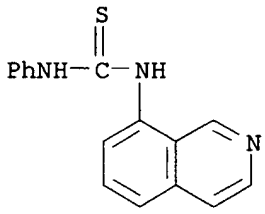
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as 5-HT1c antagonists)
RN 152239-58-2 CAPLUS
CN Urea, N-6-isoquinolinyl-N'-(1-methyl-1H-indol-5-yl)- (9CI) (CA INDEX NAME)




L5 ANSWER 19 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1989:135062 CAPLUS
DN 110:135062
TI Phenyl and isoquinolinyl derivatives of urea and thiourea
AU Nowak, K.; Poradowska, H.
CS Inst. Org. Chem. Technol., Polytech. Univ., Krakow, Pol.
SO Studies in Organic Chemistry (Amsterdam) (1988), 35(Chem. Heterocycl. Compd.), 438-40
CODEN: SOCHDQ; ISSN: 0165-3253
DT Journal
LA English
AB A lecture on the preparation and properties of Ph isoquinolinyl ureas and thioureas.
IT **119612-65-6P 119612-68-9P**
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(preparation and mass spectra of)
RN 119612-65-6 CAPLUS
CN Urea, N-8-isoquinolinyl-N'-phenyl- (9CI) (CA INDEX NAME)




RN 119612-68-9 CAPLUS
CN Thiourea, N-8-isoquinolinyl-N'-phenyl- (9CI) (CA INDEX NAME)



L5 ANSWER 20 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1980:426292 CAPLUS
DN 93:26292
TI Isoquinoline derivatives
PA Rhone-Poulenc Industries S. A., Fr.
SO Belg., 33 pp.
CODEN: BEXXAL
DT Patent
LA French
FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | BE 875797 | A1 | 19791023 | BE 1979-194791 | 19790423 |
| | FR 2424270 | A1 | 19791123 | FR 1978-12026 | 19780424 |
| | FR 2424270 | B1 | 19800919 | | |
| | FR 2449087 | A2 | 19800912 | FR 1979-4004 | 19790216 |
| | NL 7902993 | A | 19791026 | NL 1979-2993 | 19790417 |
| | AU 7946219 | A1 | 19791101 | AU 1979-46219 | 19790420 |
| | GB 2020280 | A | 19791114 | GB 1979-13821 | 19790420 |
| | GB 2020280 | B2 | 19820728 | | |
| | JP 55007260 | A2 | 19800119 | JP 1979-48895 | 19790420 |
| | ZA 7901893 | A | 19800430 | ZA 1979-1893 | 19790420 |
| | DK 7901669 | A | 19791025 | DK 1979-1669 | 19790423 |
| | SE 7903554 | A | 19791025 | SE 1979-3554 | 19790423 |
| | ES 479878 | A1 | 19800816 | ES 1979-479878 | 19790424 |
| | ES 482070 | A1 | 19800401 | ES 1979-482070 | 19790629 |
| PRAI | FR 1978-12026 | A | 19780424 | | |
| | FR 1979-4004 | A | 19790216 | | |

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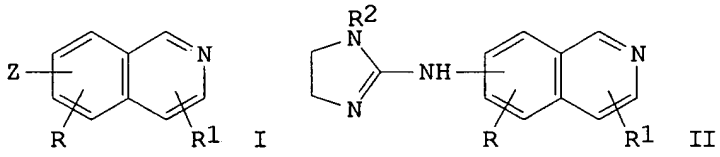
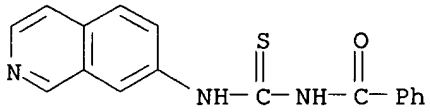


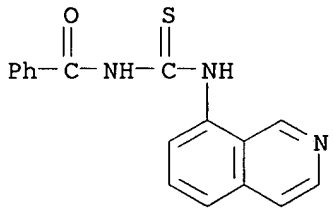

AB The cyclocondensation reaction of aminoisoquinolines I [Z (in the 4-, 5-, 6-, 7-, or 8-position) = S-alkylisothioureido, NHCS2H alkyl ester, isothiocyanato; R and R1 (same or different) are H, halo, alkyl, alkoxy, alkoxyalkyl, alkylthio, dialkylamino] with H2NCH2CH2NHR2 (R2 = H, hydroxyalkyl) gave the resp. (imidazolinylamino)isoquinolines II, useful as antihypertensives (no data). 4-(Thioureido)isoquinoline was S-methylated, and the isothiourea derivative obtained was heated 7 h with H2NCH2CH2NH2 in EtOH to give 4-[(4,5-dihydro-2-imidazolyl)amino]isoquinoline.

IT **72677-84-0P 72677-85-1P 72677-86-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and deacylation of)

RN 72677-84-0 CAPLUS
CN Benzamide, N-[(7-isoquinolinylamino)thioxomethyl]- (9CI) (CA INDEX NAME)



RN 72677-85-1 CAPLUS
CN Benzamide, N-[(8-isoquinolinylamino)thioxomethyl]- (9CI) (CA INDEX NAME)



RN 72677-86-2 CAPLUS
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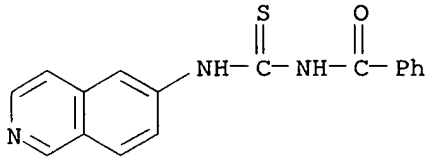

L5 ANSWER 21 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1980:111013 CAPLUS
DN 92:111013
TI Isoquinoline derivatives
IN Deprez, Dominique; Farge, Daniel; Hucherot, Jean Jaques; Moutonnier, Claude
PA Rhone-Poulenc Industries S. A., Fr.
SO Ger. Offen., 40 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | DE 2916577 | A1 | 19791031 | DE 1979-2916577 | 19790424 |
| | FR 2424270 | A1 | 19791123 | FR 1978-12026 | 19780424 |
| | FR 2424270 | B1 | 19800919 | | |
| | FR 2449087 | A2 | 19800912 | FR 1979-4004 | 19790216 |
| | NL 7902993 | A | 19791026 | NL 1979-2993 | 19790417 |
| | AU 7946219 | A1 | 19791101 | AU 1979-46219 | 19790420 |
| | GB 2020280 | A | 19791114 | GB 1979-13821 | 19790420 |
| | GB 2020280 | B2 | 19820728 | | |
| | JP 55007260 | A2 | 19800119 | JP 1979-48895 | 19790420 |
| | ZA 7901893 | A | 19800430 | ZA 1979-1893 | 19790420 |
| | DK 7901669 | A | 19791025 | DK 1979-1669 | 19790423 |
| | SE 7903554 | A | 19791025 | SE 1979-3554 | 19790423 |

| | | | | | |
|---|---|---|---|---|---|
| | ES 479878 | A1 | 19800816 | ES 1979-479878 | 19790424 |
| | ES 482070 | A1 | 19800401 | ES 1979-482070 | 19790629 |
| PRAI | FR 1978-12026 | A | 19780424 | | |
| | FR 1979-4004 | A | 19790216 | | |

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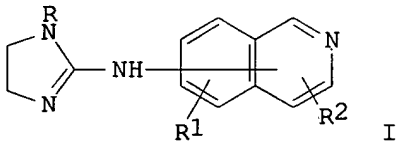
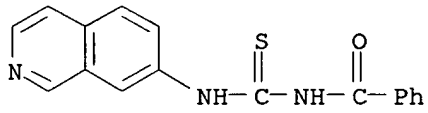


I

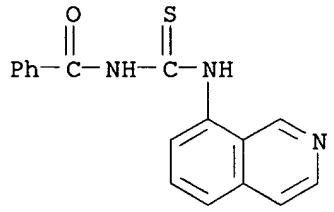
AB The antihypertensive (no data) compds. I R = H, hydroxyalkyl; R1 and R2 = H, halogen, alkyl, alkoxy, alkoxyalkyl, alkylthio, dialkylamino) and their salts were prepared Thus, 5-(2-methylisothioureido)isoquinoline-HI reacted with H2NCH2CH2NH2 in EtOH to give 4-[(4,5-dihydro-2-imidazolyl)amino]isoquinoline.

IT **72677-84-0P 72677-85-1P 72677-86-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrolysis of)

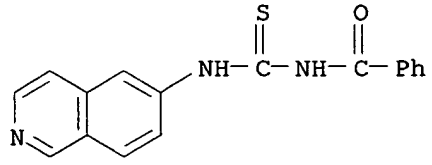
RN 72677-84-0 CAPLUS
CN Benzamide, N-[(7-isoquinolinylamino)thioxomethyl]- (9CI) (CA INDEX NAME)



RN 72677-85-1 CAPLUS
CN Benzamide, N-[(8-isoquinolinylamino)thioxomethyl]- (9CI) (CA INDEX NAME)



RN 72677-86-2 CAPLUS
CN Benzamide, N-[(6-isoquinolinylamino)thioxomethyl]- (9CI) (CA INDEX NAME)



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FULL ESTIMATED COST                              108.23     275.38

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)    SINCE FILE      TOTAL
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STN INTERNATIONAL LOGOFF AT 13:57:16 ON 24 JAN 2006
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